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(54) A BASE MATERIAL FROM WHICH TO PREPARE BONE CEMENT

(71) We, KULZER & CO., GmbH., a German Company, of 6380 Bad Homburg v.d. Höhe, Federal Republic of Germany, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:-

The invention relates to a base material from which to prepare a bone cement by admixture with a liquid monomer and a polymerisation catalyst and which contains powdered copolymers of methyl methacrylate and methyl acrylate.

Bone cements are used for example for cementing implants in position, for anchoring artificial joints in place, in the repair of skull defects, and for connecting vertebrae firmly together. Initially, the cements are prepared in the form of a plastic paste by mixing together base materials comprising powdered homopolymers or copolymers of methyl methacrylate, suitable liquid monomers, generally methyl methacrylate monomer, a polymerisation catalyst system and possibly an X-ray contrast medium such as zirconium dioxide and dyestuffs to indicate the presence of the cement in the body. This paste is then introduced into the body where it sets as a result of the polymerisation of the monomer. The polymerisation catalyst system employed is a so-called redox system. This consists of an organic peroxy compound, preferably dibenzoyl peroxide, which constitutes the catalyst, and a reducing agent (accelerator) such as dimethyl-*p*-toluidine. Thus, the bone cement disclosed in German Auslegeschrift No. 2,229,702 is prepared from polymethyl methacrylate and a monomer mixture consisting of methyl methacrylate and esters of higher alcohols of methacrylic acid, and a polymerisation catalyst system consisting of dibenzoyl peroxide and dimethyl-*p*-toluidine.

German Offenlegungsschrift 2,501,683 and British Patent No. 1505815 disclose a biologically active composite material and its use in producing a biologically active bone cement. This composite material comprises a matrix of a methacrylate-based plastics material and a biologically active substance, which stimulates the growth of the bone and which may be a glass ceramic having an apatite crystal phase, said glass ceramic consisting of 20 to 60% by weight of SiO_2, 5 to 40% by weight of P_2O_5, 2.7 to 20% by weight of Na_2O, 0.4 to 20% by weight of K_2O, 2.9 to 30% by weight of MgO and 5 to 40% by weight of CaO, as described in German Patent Specification No. 2,326,100 and British Patent No. 1441082.

To improve its mechanical properties, a fibrous material such as glass fibres may be added to the composite material disclosed in British Patent No. 1505815. If the composite material is to be used to produce a bone cement, then for example the hardener and then the fine-grain biologically active glass ceramics are added to the liquid methyl methacrylate. After polymerisation into a kneadable doughy mass, the surface of this mass may have additional powdered glass ceramics worked thereinto and it may then be introduced into the body.

In contrast to the known bone cements which are made by polymerising a mixture of polymer and monomer, the time required for polymerisation into a kneadable mass in the case of the composite material described in British Patent No. 1505815 which contains glass ceramics but which is prepared without using polymers, is too long to enable it to be used in surgical practice. In the case of known composite materials based upon polymer and monomer the time required, after mixing, to attain a mixture of suitable viscosity for introduction into the bone is considerably shorter.

Since in the case of the known composite material containing glass ceramics the monomer content thereof is higher than that of conventional bone cements based upon polymer and

monomer, there is also a danger that the monomer will be washed into the blood vessels.

The object of the invention is to provide a base material which contains two or more powdered copolymers of methyl methacrylate and methyl acrylate, for the preparation of a composite material having favourable handling characteristics, good mechanical properties after setting, and a final cement composition which promotes the growth of bone tissue.

This object is achieved in accordance with the invention by providing a base material from which to prepare a bone cement by admixture with a liquid monomer and a polymerization catalyst comprising two or more powdered copolymers of methyl methacrylate and methyl acrylate, which base material additionally contains (a) 15 to 75% by weight of an inorganic material comprising 90 to 99% by weight of a powdered biologically active glass ceramic having a particle size of 10 to 200 micrometers, and (b) 1 to 10% by weight of vitreous mineral fibres of length less than 20mm. The particle size of the biologically active glass ceramics is preferably from 90 to 125 micrometers.

A fibre content of 5 to 10% by weight and a fibre length of 1 to 10mm, preferably 2 to 5mm, have proved particularly satisfactory. The vitreous mineral fibres may be composed of a glass but are preferably composed of a biologically active glass ceramic. It is advantageous for the composition of the biologically active glass ceramics to be the same as that of the glass ceramics disclosed in British Patent Specification No. 1441082.

An antibiotic, e.g. gentamycin, may also be present in the base material according to the invention. The addition of antibiotics to bone cements is disclosed, for example, in German Offenlegungsschrift No. 2,022,117.

Test speciments produced from the peroxide-containing base material according to the invention by admixing with methyl methacrylate monomer and dimethyl-*p*-toluidine and allowing the resultant mixture to set, had greater compression strength, better impact strength and a higher modulus of elasticity than test specimens prepared from polymer/monomer mixtures or from polymer/monomer mixtures containing biologically active glass ceramics or vitreous mineral fibres.

It was surprising to find that the base material according to the invention, which comprises a mixture of two or more powdered copolymers, biologically active glass ceramics and vitreous mineral fibres, could be used to produce a bone cement having improved mechanical properties.

In the following Examples and comparative Examples there are described the production of test specimens from bone cement-producing mixtures with and without added glass ceramics and/or glass fibres.

EXAMPLE 1 (Comparative)

10 Parts by weight of a powder comprising
70 parts by weight of biologically active glass ceramics having a granule size of 90 to 125 micrometers,
26.76 parts by weight of a mixture of two or more copolymers of methyl methacrylate and methyl acrylate,
3 parts by weight of zirconium dioxide, and 0.24 parts by weight of dibenzoyl peroxide are mixed with 3 parts by weight of a liquid comprising
98 parts by weight of methyl methacrylate, and
2 parts by weight of dimethyl-*p*-toluidine.

The mixture, which becomes plastic and doughy after one minute, is moulded under pressure (3 bars) in a three-part metal mould to give pore-free test specimens. Polymerisation is complete after approximately 10 minutes.

EXAMPLE 2

10 Parts by weight of a powder comprising
65 parts by weight of biologically active glass ceramics having a granule size of 90 to 125 micrometers,
5 parts by weight of glass fibres 3 mm in length, 26.76 parts by weight of a mixture of two or more copolymers of methyl methacrylate and methyl acrylate,
3 parts by weight of zirconium dioxide, and 0.24 parts by weight of dibenzoyl peroxide are mixed with 3 parts by weight of a liquid comprising
98 parts by weight of methyl methacrylate, and
2 parts by weight of dimethyl-*p*-toluidine and the mixture is processed as described in Example 1 to produce test speciments.

EXAMPLE 3

10 Parts by weight of a powder comprising
60 parts by weight of biologically active glass ceramics having a granule size of 90 to 125 micrometers,

10 parts by weight of glass fibres 3 mm in length, 26.76 parts by weight of a mixture of two or mofe copolymers of methyl methacrylate and methyl acrylate, 3 parts by weight of zirconium dioxide, and
0.24 parts by weight of dibenzoyl peroxide are mixed with 3 parts by weight of a liquid comprising
98 parts by weight of methyl methacrylate, and
2 parts by weight of dimethyl-*p*-toluidine and the mixture is processed as described in Example 1 to produce test specimens.

EXAMPLE 4 (Comparative)

10 Parts by weight of a powder comprising
96.76 parts by weight of a mixture of two or more copolymers of methyl methacrylate and methyl acrylate,
3 parts by weight of zirconium dioxide, and
0.24 parts by weight of dibenzoyl peroxide are mixed with 5 parts by weight of a liquid comprising
98 parts by weight of methyl methacrylate, and
2 parts by weight of dimethyl-*p*-toluidine and the mixture is processed as described in Example 1 to produce test specimens.

EXAMPLE 5 (Comparative)

10 Parts by weight of a powder comprising
91.76 parts by weight of a mixture of two or more copolymers of methyl methacrylate and methyl acrylate,
5 parts by weight of glas fibres 3 mm in length
3 parts by weight of zirconium dioxide, and
0.24 parts by weight of dibenzoyl peroxide
are mixed with 5 parts by weight of a liquid comprising
98 parts by weight of methyl methacrylate, and
2 parts by weight of dimethyl-*p*-toluidine
and the mixture is processed as described in Example 1 to produce test specimens.

EXAMPLE 6

10 Parts by weight of a powder comprising
65 parts by weight of biologically active glass ceramics having a granule size of 90 to 125 micrometers
5 parts by weight of glass fibres 3 mm in length, 26.76 parts by weight of a mixture of two or more copolymers of methyl methacrylate and methyl acrylate,
3 parts by weight of zirconium dioxide,
0.24 parts by weight of dibenzoyl peroxide,
2.12 parts by weight of gentamycin sulphate
are mixed with 3 parts by weight of a liquid comprising
98 parts by weight of methyl methacrylate, and
2 parts by weight of dimethyl-*p*-toluidine
and the mixture is processed as described in Example 1 to produce test specimens.

EXAMPLE 7

10 Parts by weight of a powder comprising
60 parts by weight of biologically active glass ceramics having a granule size of 90 to 125 micrometers,
10 parts by weight of glass fibres 3 mm in length,
26.76 parts by weight of a mixture of two or more copolymers of methyl methacrylate and methyl acrylate,
3 parts by weight of zirconium dioxide,
0.24 parts by weight of dibenzoyl peroxide, and
2.12 parts by weight of gentamycin sulphate
are mixed with 3 parts by weight of a liquid comprising
98 parts by weight of methyl methacrylate, and
2 parts by weight of dimethyl-*p*-toluidine
and the mixture is processed as described in Example 1 to produce test specimens.

EXAMPLE 8 (Comparative)

10 Parts by weight of a mixture comprising
96.76 parts by weight of a mixture of two or more copolymers of methyl methacrylate and methyl acrylate,
3 parts by weight of zirconium dioxide,

0.24 parts by weight of dibenzoyl peroxide, and
2.12 parts by weight of gentamycin sulphate
are mixed with 5 parts by weight of a liquid comprising
98 parts by weight of methyl methacrylate, and
2 parts by weight of dimethyl-*p*-toluidine
and the mixture is processed as described in Example 1 to produce test specimens.

The values given in the Table for certain mechanical properties of the test specimens show that the test specimens produced using the base material according to the present invention exhibit high values for impact strength and modulus of elasticity.

As has already been indicated above, an antibiotic may be added to the base material according to the present invention. Of the many possible antibiotics the following may be mentioned as examples: aminoglycoside antibiotics, such as amikacin, butirosin, didesoxykanamycin B (DKB), fortimycin, gentamycin, kanamycin, lividomycin, neomycin, netilmicin, ribostamycin, sagamycin, seldomycin and its epimers, sisomicin, sorbistin and tobramycin; chloramphenicol and its derivatives such as thiamphenicol; ethythromycins; lactone antibiotics such as novobiocin; leucomycins such as josamycin, maridomycin, midecamycin, spiramycin; lincomycins such as clindamycin and lincomycin; macrolides such as rosamicin; penicillins such as amoxicillin, ampicillin, sodium azlicillon, sodium dicloxacillin, furoxacillin, mecillinam, and piperacillin; peptide antibiotics such as bacitracin, sodium colistimethate, gramicidin and polymyxin; rifamycins such as rifampicin and rifamycin; steroid antibiotics such as fusidic acid; streptomycins; tetracyclins such as doxycyclin, minocyclin and tetracyclin; cephalosporins such as cefalotin, cefamandol, cefazedon, cefazolin, cefoxitin and cefuroxim; and other antibiotics such as cycloserin, fosfomycin and vancomycin. The aminoglycoside antibiotics, in particular gentamycin, are particularly suitable because of their wide antibacterial spectrum and their stability when heated.

TABLE

Test Specimens	Impact Strength [kJ / m^2]	Bending Strength [N / mm]	Compression Strength [M Pa]	Modulus of Elasticity
As in Example 1 (Comparative)	0.78	38.3	76	45.10^2
As in Example 2 (according to the invention)	7.50	59.8	87	52.10^2
As in Example 3 (according to the invention)	11.6	70.0	96	67.10^2
As in Example 4 (Comparative	4-5	60-80	82-85	20.10^2
As in Example 5 (Comparative)	6.0	71.0	-	-
As in Example 6 (according to the invention)	4.36	58.1	82	50.10^2
As in Example 7 (according to the invention)	8.58	70.2	87	65.10^2
As in Example 8 (Comparative)	1.32	46.8	-	-

WHAT WE CLAIM IS:-

1. A base material from which to prepare a bone cement by admixture with a liquid monomer and a polymerisation catalyst comprising two or more powdered copolymers of methyl methacrylate and methyl acrylate, which material additionally contains (a) 15 to 75% by weight of an inorganic material comprising 90 to 99% by weight of a powdered biologically active glass ceramic having a particle size of 10 to 200 micrometers, and (b) 1 to 10% by weight of vitreous mineral fibres having a length of less than 20 mm.

2. A base material according to claim 1, in which said inorganic material contains 5 to 10% by weight of said vitreous mineral fibres.

3. A base material according to either of claims 1 or 2, in which the length of said vitreous mineral fibres is 1 to 10 mm.

4. A base material according to claim 3, in which the length of said vitreous mineral fibres is 2 to 5 mm.

5. A base material according to any of the preceding claims, in which the particle size of the powdered biologically active glass ceramics is 90 to 125 micrometers.

6. A base material according to any of the preceding claims, in which the vitreous mineral fibres are glass fibres.

7. A base material according to one of claims 1 to 5, in which said vitreous mineral fibres are biologically active glass ceramic fibres.

8. A base material according to claim 7, in which said fibres are composed of biologically active glass ceramic comprising 20 to 60% by weight of Sio_2, 5 to 40% by weight of P_2O_5, 2.7 to 20% by weight of Na_2O, 0.4 to 20% by weight of K_2O, 2.9 to 30% by weight of MgO and 5 to 40% by weight of CaO.

9. A base material according to any of the preceding claims, in which the powdered biologically active glass ceramic comprises 20 to 60% by weight of SiO_2, 5 to 40% by weight of P_2O_5, 2.7 to 20% by weight of Na_2O, 0.4 to 20% by weight of K_2O, 2.9 to 30% by weight of MgO and 5 to 40% by weight of CaO.

10. A base material according to any of the preceding claims, which also contains a polymerisation catalyst.

11. A base material according to claim 10, in which the polymerisation catalyst is a peroxy compound.

12. A base material according to any of the preceding claims, which also contains an X-ray contrast medium.

13. A base material according to claim 12, in which the X-ray contrast medium is zirconium dioxide.

14. A base material according to one or more of the foregoing claims, which also contains an antibiotic.

15. A base material from which to prepare a bone cement according to claim 1 and substantially as hereinbefore described with reference to any of Examples 2, 3, 6 or 7.

16. Implantable shaped bodies which have been made by the polymerisation of a base material according to any of the claims 1-15, a monomer and a polymerisation catalyst.

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